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=> adjuvant
L1 85701 ADJUVANT

=> ribavirin
L2 8756 RIBAVIRIN

=> L1 and L2
L3 58 L1 AND L2

=> HCV
L4 32431 HCV

=> L3 and L4
L5 16 L3 AND L4

=> D L5 IBIB ABS 1-16

L5 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:451523 CAPLUS
DOCUMENT NUMBER: 143:2205
TITLE: Methods for modifying sequences encoding hepatitis C virus glycoproteins and therapeutic uses thereof
INVENTOR(S): Cormier, Emmanuel G.; Gardner, Jason; Dragic, Tatjana; Dumonceaux, Julie
PATENT ASSIGNEE(S): Progenics Pharmaceuticals, Inc., USA; Albert Einstein College of Medicine of Yeshiva University
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005047481	A2	20050526	WO 2004-US37693	20041109
WO 2005047481	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005266400	A1	20051201	US 2004-985205	20041109
PRIORITY APPLN. INFO.:			US 2003-519536P	P 20031112

AB The present invention concerns a modified nucleic acid mol. comprising a nucleotide sequence coding for a full length hepatitis C virus (**HCV**) glycoprotein selected from the group consisting of E1 glycoprotein and E1/E2 glycoprotein heterodimer, this mol. having at least one nucleotide alteration, wherein, due to this alteration, at least one RNA splice site selected from the group consisting of RNA splice acceptor and RNA splice donor sites is eliminated from the coding sequence. The invention is also directed to methods for expressing on the surface of a cell and a pseudovirion an **HCV** glycoprotein, wherein the majority of the glycoprotein is full length. The invention further provides a cell and a pseudovirion expressing such glycoprotein. The invention still further provides a method for determining whether an agent inhibits **HCV** fusion with and entry into a target cell. The invention also provides an agent that inhibits **HCV** fusion with and entry into a target cell. The invention further provides methods for

treating a subject afflicted with an **HCV**-associated disorder, for preventing an **HCV** infection in a subject, and for inhibiting in a subject the onset of an **HCV**-associated disorder.

L5 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409553 CAPLUS
DOCUMENT NUMBER: 142:459118
TITLE: **HCV** NS3-NS4A protease resistance mutants affecting the activity of NS3-NS4A inhibitory drugs VX-950 and BILN2061 and structure-based anti-**HCV** drug design
INVENTOR(S): Lin, Chao; Lin, Kai
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042570	A1	20050512	WO 2004-US35839	20041027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005136400	A1	20050623	US 2004-974558	20041027
PRIORITY APPLN. INFO.:			US 2003-514740P P	20031027
			US 2003-525222P P	20031126
			US 2004-561662P P	20040413

AB The present invention is directed to mutants of **HCV** NS3/4A protease. More particularly, the present invention identifies mutant of **HCV** NS3/4A protease that are resistant to drug treatment. In particular embodiments, in vitro resistance studies of NS3·4A mutants at the residues Ala156 and Asp168 of NS3·4A protease domain using a subgenomic replicon system to compare VX-950 with another **HCV** NS3.4A protease inhibitor, BILN 2061, are reported. Distinct drug-resistant substitutions, including Ala156 to Ser or Val or Thr, and Asp168 to Glu or Val or Ala or Gly or Tyr, are identified in the **HCV** NS3 serine protease domain for both inhibitors. The resistance conferred by these mutations is confirmed by characterization of the mutant enzymes and replicon cells that contain the single amino acid substitutions. The major BILN 2061-resistant mutations at Asp168 are fully susceptible to VX-950, and the dominant resistant mutation against VX-950 at Ala156 remains sensitive to BILN 2061. Modeling anal. suggests that there are different mechanisms of resistance to VX-950 and BILN 2061.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:133403 CAPLUS
DOCUMENT NUMBER: 142:441317
TITLE: Etanercept as an **adjuvant** to interferon and **ribavirin** in treatment-naive patients with chronic hepatitis C virus infection: a phase 2 randomized, double-blind, placebo-controlled study
AUTHOR(S): Zein, Nizar N.
CORPORATE SOURCE: Etanercept Study Group, Division of Gastroenterology and Hepatology and Internal Medicine, Mayo Clinic, Rochester, MN, USA
SOURCE: Journal of Hepatology (2005), 42(3), 315-322

CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background/Aims: Current therapies for patients with chronic hepatitis C virus (**HCV**) do not achieve sustained viral clearance in most patients, and are associated with severe toxic effects. Our aim was to investigate the efficacy and safety of etanercept as **adjuvant** to interferon and **ribavirin** in treatment-naive patients with **HCV**. Methods: Double-blind, randomized, placebo controlled trial. Fifty patients with chronic **HCV** were randomly assigned to receive interferon alfa-2b and **ribavirin** with either etanercept or placebo for 24 wk. The main outcome measure was the absence of **HCV** RNA at 24 wk, the on treatment response at the end of the etanercept randomization period. Results: At 24 wk, **HCV** RNA was absent in 63% (12/19) etanercept patients compared to 32% (8/25) placebo patients (P=0.04). In addition, patients receiving etanercept had lower frequency of most adverse events categories compared to placebo. Conclusions: Etanercept given for 24 wk as **adjuvant** therapy to interferon and **ribavirin** significantly improved virol. response at the end of the etanercept randomization period among patients with **HCV**, and was associated with decreased incidence of most adverse effects associated with interferon and **ribavirin**.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:999666 CAPLUS
DOCUMENT NUMBER: 141:423308
TITLE: Vaccines containing **adjuvant ribavirin** and **HCV** antigene NS3 and NS4A for treating infection by hepatitis C virus
INVENTOR(S): Sallberg, Matti; Hultgren, Forsberg Catharina
PATENT ASSIGNEE(S): Swed.
SOURCE: U.S. Pat. Appl. Publ., 93 pp., Cont.-in-part of U.S. Ser. No. 719,619.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004229832	A1	20041118	US 2004-817591		20040402
US 2002136740	A1	20020926	US 2001-929955		20010815
US 6858590	B2	20050222			
US 2002155124	A1	20021024	US 2002-104966		20020322
US 6680059	B2	20040120			
US 2004086529	A1	20040506	US 2003-719619		20031120
PRIORITY APPLN. INFO.:			US 2000-225767P	P	20000817
			US 2000-229175P	P	20000829
			US 2000-705547	B1	20001103
			US 2001-929955	A1	20010815
			US 2002-104966	A1	20020322
			US 2003-719619	A2	20031120

AB Compns. and methods for enhancing the effect of vaccines in animals, such as domestic, sport, or pet species, and humans are disclosed. More particularly, vaccine compns. comprising **ribavirin** and an antigen, preferably an antigen that has an epitope present in Hepatitis C virus (**HCV**), are disclosed for use in treating and preventing disease, preferably **HCV** infection. The data demonstrate that **ribavirin** facilitates or enhances an immune response to an **HCV** antigen or **HCV** epitopes. A potent immune response to rNS3 was elicited after immunization with a vaccine composition comprising as little as 1 mg **ribavirin** and 10 μg of rNS3 antigen. The data further verify that **ribavirin** can be administered as an **adjuvant** and establish that that the dose of **ribavirin** can modulate the kinetics of the **adjuvant** effect.

L5 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:997248 CAPLUS
TITLE: Hepatitis C vaccines to prevent liver cancer
AUTHOR(S): Houghton, M.
CORPORATE SOURCE: Chiron Corporation, Emeryville, CA, USA
SOURCE: Developments in Biologicals (Basel, Switzerland) (2004), 116(Development of Therapeutic Cancer Vaccines), 191-192
CODEN: DBEIAI; ISSN: 1424-6074
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The hepatitis C virus (**HCV**) infects .apprx. 170 million individuals world-wide with a substantial annual incidence of new infections. At least 50% of infections become persistent and while most are relatively asymptomatic, there is a significant risk of a sequential progression to chronic active hepatitis, liver cirrhosis and then hepatocellular carcinoma (HCC). In Japan, **HCV** is the major risk factor for HCC. In essentially all cases, HCC is preceded by liver cirrhosis indicating that the latter is an absolute requirement for **HCV**-associated liver cancer development. Various viral factors have also been postulated to be directly involved. Possible approaches to preventing **HCV**-related HCC include the development of a prophylactic vaccine to prevent the development of persistent infection following virus exposure, as well as therapeutic vaccines to either slow the progression of liver disease or to eradicate viral infection through the boosting of viral-specific humoral and cellular immune responses. Since the outcome of the standard-of-care treatment for chronic **HCV** patients (a combination of interferon-alpha and the guanosine analog **ribavirin**) appears to be dependent in part on the quality and quantity of both **HCV**-specific humoral and cellular immune responses, a therapeutic vaccine may be most effective when used as an adjunct with these and future antiviral drugs. A prophylactic vaccine comprising recombinant envelope glycoproteins E1 and E2 has been shown to prevent the development of persistent infection following exptl. challenge with both homologous and heterologous viral inocula in vaccinated chimpanzees, which represent the only animal model available. A related vaccine formulation is about to enter clin. trials in the USA. This vaccine primes the induction of anti-envelope antibodies as well as CD4+ T helper responses and may also be of value in treating chronically-infected patients with liver disease. In addition, we have been investigating methods to prime and boost **HCV**-specific cytotoxic lymphocytes (CTLs) capable of killing infected hepatocytes as well as secreting antiviral cytokines which are therefore of potential therapeutic value. One effective method is the combination of the ISCOMs **adjuvant** (CSL Ltd) with a variety of recombinant **HCV** proteins. In rhesus macaques, a core protein adjuvanted with ISCOMs was shown to be very effective at priming core-specific Th1-like CD4+ T cells as well as CD8+ CTLs. Recently, this work has been extended to a large yeast-derived **HCV** polyprotein comprising the nonstructural proteins 3, 4 & 5 fused to the core protein. When adjuvanted with ISCOMs, strong multispecific T helper and CTL responses have been elicited in vaccinated chimpanzees that were superior to those elicited by various **HCV** DNA vaccine formulations.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:846584 CAPLUS
DOCUMENT NUMBER: 142:147589
TITLE: Past, present, and future hepatitis C treatments
AUTHOR(S): Foster, Graham R.
CORPORATE SOURCE: Hepatobiliary Group, Department of Adult and Paediatric Gastroenterology, Queen Marys School of Medicine and Dentistry, London, UK
SOURCE: Seminars in Liver Disease (2004), 24(Suppl. 2), 97-104
CODEN: SLDIEE; ISSN: 0272-8087
PUBLISHER: Thieme Medical Publishers, Inc.

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Conventional interferon (IFN) alfa has been used for many years in the treatment of chronic hepatitis C. However, few patients achieve sustained virol. responses with IFN. Combining IFN with **ribavirin** improves efficacy considerably, but at the expense of diminished tolerability attributable to **ribavirin**. Pegylated interferons have improved pharmacokinetic profiles, may be administered once weekly, and are more effective than IFN is alone or in combination with **ribavirin**. In addition to enhanced efficacy, pegylated interferon alfa-2a (40 kD) also improves health-related quality of life during therapy compared with IFN-based therapy. New **adjuvant** agents have the potential to further improve sustained response rates and tolerability; however, pegylated interferons will likely remain the backbone of therapy in the foreseeable future. Therapies under development and evaluation for patients with **HCV** infection include adjunctive use of the antiviral agent amantadine and the immunomodulatory agent thymalfasin. Novel small mols. include the **ribavirin** analogs, viramidine and levovirin, and BILN 2061, an inhibitor of **HCV** serine protease. Other therapeutic strategies that have reached the clinic include antisense oligonucleotides (ISIS 14803), nuclease-resistant ribozymes targeting **HCV** RNA (Heptazyme), human monoclonal antibodies, and human antibody fragments directed at **HCV** helicase.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

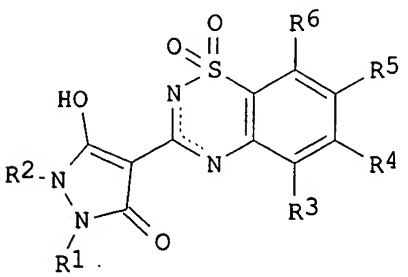
L5 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:566539 CAPLUS
DOCUMENT NUMBER: 141:128820
TITLE: Anti-infective compositions for hepatitis C virus
INVENTOR(S): Fitch, Duke M.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058150	A2	20040715	WO 2003-US40133	20031211

W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, EG, GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, TN, TT, UA, US, UZ, VN, YU, ZA

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-434227P P 20021217
OTHER SOURCE(S): MARPAT 141:128820
GI



I

AB The present invention provides compds. useful as **HCV** anti-infectives having the formula (I) wherein R1 and R2 are each independently selected from the group consisting of: C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C8 cycloalkyl, aryl or heteroaryl, etc; R3 is hydrogen, halogen, cyano, C1-C6 alkyl, -OH, or -OC1-C4 alkyl, etc; R4 is hydrogen, halogen, cyano, C1-C6 alkyl, -OH, -OC1-C4 alkyl, C1-C4 haloalkyl, nitro or amino, etc; R5 is H, nitro, cyano, halogen, -C(O)OR7, -C(O)R7, -OR7, -SR7, -S(O)R7, -S(O)2R7, -NR8R9, etc; R6 is H, halogen, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, -OR7, -SR7, -NR8R9, cyano or nitro, etc. Also disclosed are methods of making and using the same.

L5 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:520712 CAPLUS
DOCUMENT NUMBER: 141:331271
TITLE: Tomato-based functional food as interferon **adjuvant** in **HCV** eradication therapy
AUTHOR(S): Morisco, Filomena; Vitaglione, Paola; Carbone, Antonella; Stingo, Stefania; Scarpati, Sergio; Ascione, Antonio; Marmo, Riccardo; Fogliano, Vincenzo; Caporaso, Nicola
CORPORATE SOURCE: Department of Food Science, University of Naples, Federico II, Italy
SOURCE: Journal of Clinical Gastroenterology (2004), 38(6, Suppl. 2), S118-S120
CODEN: JCGADC; ISSN: 0192-0790
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB GOALS: The authors conducted a study to verify whether supplementation with an antioxidant-rich tomato-based functional food reduces anemia during pegylated interferon and **ribavirin** therapy for chronic hepatitis C. BACKGROUND: Oxidative stress plays a major role in the physiopathol. of hemolytic anemia during **ribavirin** therapy. The efficacy of antioxidant supplementation with vitamins C and E as pure compds., is still controversial. METHODS: A functional food with a high content of natural antioxidants and with high carotenoid bioavailability was developed. The authors enrolled 92 patients with chronic hepatitis C, treated with standard combination therapy. Forty-six of them received a daily dose (100 g) of functional food (group 1), and 46 did not (group 2). The effect of antioxidant activity was assessed comparing compliance with the full dose of **ribavirin** and Hb levels during the first 3 mo of treatment. RESULTS: Only 8.7% of patients in group 1 had to reduce their daily **ribavirin** dose, whereas **ribavirin** reduction was necessary for 30.4% of patients in group 2 (P = 0.09). Hb levels showed significant differences at 15, 30, and 90 days during the observation time. CONCLUSION: Results demonstrated that the authors' functional food reduces the severity of **ribavirin**-related anemia and improves the tolerance to the full dose of **ribavirin** in patients with chronic hepatitis C.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:513502 CAPLUS
DOCUMENT NUMBER: 141:59738
TITLE: Anti-infectives compounds and use for treating hepatitis C virus infection associated diseases
INVENTOR(S): Chai, Deping; Duffy, Kevin J.; Fitch, Duke M.; Shaw, Antony N.; Tedesco, Rosanna; Wiggall, Kenneth J.; Zimmerman, Michael N.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052312	A2	20040624	WO 2003-US39982	20031211

W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, EG, GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, TN, TT, UA, US, UZ, VN, YU, ZA

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-432413P P 20021211

AB The present invention relates to compds. that inhibit an RNA-containing virus hepatitis C virus (**HCV**) and methods of making and using the same.

L5 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:874780 CAPLUS

DOCUMENT NUMBER: 139:363583

TITLE: Non-structural ns3/4a fusion gene from hepatitis C virus optimized for codons most frequently used in humans, and uses in immunogenic preparations

INVENTOR(S): Sallberg, Matti

PATENT ASSIGNEE(S): Swed.

SOURCE: U.S. Pat. Appl. Publ., 83 pp., Cont.-in-part of U.S. Ser. No. 930,591.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003206919	A1	20031106	US 2002-307047	20021126
US 2002136740	A1	20020926	US 2001-929955	20010815
US 6858590	B2	20050222		
US 2004092730	A1	20040513	US 2001-930591	20010815
US 6960569	B2	20051101		
CA 2506820	AA	20040610	CA 2003-2506820	20031125
WO 2004048402	A2	20040610	WO 2003-IB6361	20031125
WO 2004048402	A3	20040729		
WO 2004048402	B1	20041007		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1567190	A2	20050831	EP 2003-782748	20031125

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE, HU, SK

US 2005124573	A1	20050609	US 2005-43808	20050125

PRIORITY APPLN. INFO.:

US 2000-225767P	P	20000817
US 2000-229175P	P	20000829
US 2001-929955	A2	20010815
US 2001-930591	A2	20010815
US 2002-307047	A	20021126
WO 2003-IB6361	W	20031125

AB Aspects of the present invention relate to the discovery of a novel hepatitis C virus (**HCV**) strain isolated from a human patient. This **HCV** isolate has a naturally occurring fusion protein of non-structural proteins NS3/4a. The chimeric gene for the fusion protein was found to be significantly more effective at stimulating an antigenic response than the gene for NS3 alone. Mutants of the NS3/4A peptide were

also created and were found to be immunogenic. Addnl. embodiments include a NS3/4A encoding nucleic acid or corresponding peptide, which comprise a sequence that was optimized for codons most frequently used in humans. The codon optimized nucleic acid was found to generate a higher expression level of NS3 and was found to be more immunogenic, with respect to both humoral and cellular responses, as compared to the native NS3/4A gene. Embodiments include **HCV** peptides, nucleic acids encoding said **HCV** peptides, antibodies directed to said peptides, compns. containing said nucleic acids and peptides, as well as methods of making and using the aforementioned compns. including, but not limited to, diagnostics and medicaments for the treatment and prevention of **HCV** infection.

L5 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:511157 CAPLUS
DOCUMENT NUMBER: 139:73987
TITLE: **Ribavirin** granulate for producing film-coated tablets
INVENTOR(S): Sobel, Cornelius; Huber, Gerald
PATENT ASSIGNEE(S): Biopartners G.m.b.H., Switz.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053450	A1	20030703	WO 2001-EP15202	20011221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2470342	AA	20030703	CA 2001-2470342	20011221
AU 2002229678	A1	20030709	AU 2002-229678	20011221
EP 1455801	A1	20040915	EP 2001-990585	20011221
EP 1455801	B1	20050309		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 290387	E	20050315	AT 2001-990585	20011221
NZ 533808	A	20050324	NZ 2001-533808	20011221
US 2005123612	A1	20050609	US 2003-499783	20011221
ES 2238497	T3	20050901	ES 2001-1990585	20011221
JP 2006502961	T2	20060126	JP 2003-554207	20011221

PRIORITY APPLN. INFO.:
EP 2001-990585 A 20011221
WO 2001-EP15202 W 20011221

AB The invention relates to a method for producing a granulate containing **ribavirin**. The method comprises: the production of a granulate solution, which involves the mixing of binding agents with an isopropanol/water or ethanol/water mixture, blending the granulate solution with a mixture of **ribavirin** powder and a hydrophilic or swellable solid **adjuvant** and screening and drying the granulate that has been obtained. The method is characterized in that the fraction of isopropanol or ethanol in the alc./water mixture is between 65 and 85 weight %. The granulate forms the basis for the production of a **ribavirin** tablet, which can be used for treating diseases such as, among others, **HCV** . Thus a tablet contained (mg): **ribavirin** 200.00; Polyvidon K25 16.00; microcryst. cellulose 77.00; Crospovidon 3.50; silica 2.00; magnesium stearate 1.60. The coating included per tablet (mg): hydroxypropylmethylcellulose 4.00; titanium dioxide 2.00.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:142750 CAPLUS
DOCUMENT NUMBER: 136:196947
TITLE: A naturally occurring fusion protein of non-structural proteins NS3/4a of hepatitis C virus for use as an antigen in vaccines
INVENTOR(S): Sallberg, Matti
PATENT ASSIGNEE(S): Tripep AB, Swed.
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014362	A2	20020221	WO 2001-IB1774	20010815
WO 2002014362	A3	20031113		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090178	A5	20020225	AU 2001-90178	20010815

PRIORITY APPLN. INFO.:		
US 2000-225767P	P	20000817
US 2000-229175P	P	20000829
US 2000-705547	A	20001103
WO 2001-IB1774	W	20010815

AB Disclosed herein is the discovery of a novel hepatitis C virus (**HCV**) isolated from a human patient. Embodiments of the invention include **HCV** peptides, nucleic acids encoding said **HCV** peptides, antibodies directed to said peptides, compns. containing said nucleic acids and peptides, as well as, methods of making and using the aforementioned compns. including, but not limited to, diagnostics and medicaments for the treatment and prevention of **HCV** infection. The chimeric gene for the fusion protein was found to be significantly more effective at stimulating an antigenic response than the gene for NS3 alone.

L5 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:142545 CAPLUS
DOCUMENT NUMBER: 136:198914
TITLE: Vaccines containing **ribavirin** as **adjuvant**
INVENTOR(S): Sallberg, Matti; Hultgren, Catharina
PATENT ASSIGNEE(S): Tripep AB, Swed.
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002013855	A2	20020221	WO 2001-IB1808	20010815
WO 2002013855	A3	20030109		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2419418	AA	20020221	CA 2001-2419418	20010815
AU 2001092151	A5	20020225	AU 2001-92151	20010815
EP 1311289	A2	20030521	EP 2001-972379	20010815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004506018	T2	20040226	JP 2002-518994	20010815
PRIORITY APPLN. INFO.:			US 2000-225767P P	20000817
			US 2000-229175P P	20000829
			US 2000-705547 A	20001103
			WO 2001-IB1808 W	20010815

AB Compns. and methods for enhancing the effect of vaccines in animals, such as domestic, sport, or pet species, and humans are disclosed. More particularly, vaccine compns. comprising **ribavirin** and an antigen, preferably an antigen that has an epitope present in hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (**HCV**) are disclosed for use in treating and preventing disease, preferably HAV, HBV and **HCV** infection.

L5 ANSWER 14 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:193768 BIOSIS
DOCUMENT NUMBER: PREV200500196964
TITLE: Etanercept as an **adjuvant** to interferon and **ribavirin** in treatment-naive patients with chronic hepatitis C virus infection: a phase 2 randomized, double-blind, placebo-controlled study.
AUTHOR(S): Etanercept Study Grp [Reprint Author]
CORPORATE SOURCE: Div Gastroenterol and Hepatol and Internal Med, Mayo Clin, Rochester, MN, USA
SOURCE: Journal of Hepatology, (March 2005) Vol. 42, No. 3, pp. 315-322. print.
ISSN: 0168-8278 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 May 2005
Last Updated on STN: 25 May 2005

AB Background/Aims: Current therapies for patients with chronic hepatitis C virus (**HCV**) do not achieve sustained viral clearance in most patients, and are associated with severe toxic effects. Our aim was to investigate the efficacy and safety of etanercept as **adjuvant** to interferon and **ribavirin** in treatment-naive patients with **HCV**. Methods: Double-blind, randomized, placebo controlled trial. Fifty patients with chronic **HCV** were randomly assigned to receive interferon alfa-2b and **ribavirin** with either etanercept or placebo for 24 weeks. The main outcome measure was the absence of **HCV** RNA at 24 weeks, the on treatment response at the end of the etanercept randomization period. Results: At 24 weeks, **HCV** RNA was absent in 63 % (12/19) etanercept patients compared to 32 % (8/25) placebo patients (P = 0.04). In addition, patients receiving etanercept had lower frequency of most adverse events categories compared to placebo. Conclusions: Etanercept given for 24 weeks as **adjuvant** therapy to interferon and **ribavirin** significantly improved virologic response at the end of the etanercept randomization period among patients with **HCV**, and was associated with decreased incidence of most adverse effects associated with interferon and **ribavirin**.

L5 ANSWER 15 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:106681 BIOSIS
DOCUMENT NUMBER: PREV200000106681
TITLE: Perspectives for a vaccine against hepatitis C virus.
AUTHOR(S): Abrignani, Sergio [Reprint author]; Houghton, Michael; Hsu, Henry H.
CORPORATE SOURCE: Chiron Research Center, IRIS, Via Fiorentina 1, 53100,

Siena, Italy
SOURCE: Journal of Hepatology, (1999) Vol. 31, No. Suppl. 1, pp. 259-263. print.
CODEN: JOHEEC. ISSN: 0168-8278.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Mar 2000
Last Updated on STN: 3 Jan 2002

AB There is no vaccine for **HCV** and the only available treatment, IFNalpha alone or in combination with **ribavirin**, has proven efficacious in less than 50% of patients. Given that approximately 200 million chronic **HCV** infections have been estimated worldwide, there is a pressing need to develop vaccination strategies aimed at preventing and possibly eradicating **HCV** infection. However, several major practical and scientific problems arise in designing an **HCV** vaccine. First, **HCV** is only readily detected as RNA by PCR. Second, the only species that can be infected by **HCV** are humans and chimpanzees. Third, the virus does not replicate efficiently in vitro. Fourth, some viral proteins have very high mutability. Last, there is little information on correlates of immunity. Although an ideal vaccine should protect from infection, in that it should elicit sterilizing immunity, this is quite an ambitious goal in the PCR era. In the case of **HCV**, where acute **HCV** infection is a very limited health problem and infection can only be assessed by PCR, a more realistic goal might be to look for vaccines capable of protecting from chronic infection. We have preliminary evidence in chimpanzees that an **HCV** vaccine consisting of recombinant envelope proteins can elicit antibodies and inflammatory CD4+ T cell responses which can prevent chronic infection in the majority of vaccinees. Although the scientific and clinical challenges that need to be addressed are still substantial, advances in recombinant protein technology, novel **adjuvants**, and DNA vaccines, will be key in developing strategies to generate protective immunity against chronic **HCV** infection.

L5 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:493548 BIOSIS
DOCUMENT NUMBER: PREV199799792751
TITLE: Chronic hepatitis C.
AUTHOR(S): Sharara, Ala I.
CORPORATE SOURCE: Div. Gastroenterol., Duke Univ. Med. Center, Box 3083, Durham, NC 27710, USA
SOURCE: Southern Medical Journal, (1997) Vol. 90, No. 9, pp. 872-877.
CODEN: SMJOAV. ISSN: 0038-4348.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 1997
Last Updated on STN: 7 Nov 1997

AB Background. Infection with the hepatitis C virus (**HCV**) is a leading cause of chronic liver disease worldwide. Epidemiologic and natural history studies have helped to define the clinical impact of **HCV** infection, and molecular diagnostic assays have established clinical endpoints against which therapeutic regimens are currently tested. The absence of definitive therapy has generated controversy regarding indications and optimal candidacy for currently approved treatment. This paper reviews the epidemiology, natural history, clinical manifestations, diagnostic modalities, and current treatment of chronic **HCV** infection. Methods. Search of the MEDLINE database for English-language articles and abstracts on chronic **HCV** infection yielded data from more than 500 original papers, reviews, and abstracts. Results and Conclusions. Hepatitis C virus is transmitted primarily through contaminated blood and less effectively by human body secretions, but a large proportion of patients have no clearly identifiable parenteral risk factors for viral acquisition. Infection with **HCV** results in subclinical chronic hepatitis in the majority of patients and may progress, usually over decades, to cirrhosis and hepatocellular carcinoma. Extrahepatic manifestations of **HCV** infection include porphyria

cutanea tarda, mixed essential cryoglobulinemia, and membranoproliferative glomerulonephritis. Diagnostic modalities are accurate in estimating viral load and genotype and may be helpful in predicting and assessing response to treatment. Current therapy is limited to interferon alfa and is effective at viral eradication in only a small number of patients. The **adjuvant** use of drugs, such as **ribavirin**, in combination with interferon may hold promise at enhancing viral eradication. Understanding the mechanisms behind viral persistence and immune escape of **HCV** will be essential in developing effective future therapeutic and preventive strategies.

=> humoral (s) immune
L6 22151 HUMORAL (S) IMMUNE

=> L3 and L6
L7 2 L3 AND L6

=> cellular (s) immune
L8 25496 CELLULAR (S) IMMUNE

=> L8 and l3
L9 2 L8 AND L3

=> D L7 IBIB ABS 1-2

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:997248 CAPLUS
TITLE: Hepatitis C vaccines to prevent liver cancer
AUTHOR(S): Houghton, M.
CORPORATE SOURCE: Chiron Corporation, Emeryville, CA, USA
SOURCE: Developments in Biologicals (Basel, Switzerland) (2004), 116(Development of Therapeutic Cancer Vaccines), 191-192
CODEN: DBEIAI; ISSN: 1424-6074
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The hepatitis C virus (HCV) infects .apprx. 170 million individuals world-wide with a substantial annual incidence of new infections. At least 50% of infections become persistent and while most are relatively asymptomatic, there is a significant risk of a sequential progression to chronic active hepatitis, liver cirrhosis and then hepatocellular carcinoma (HCC). In Japan, HCV is the major risk factor for HCC. In essentially all cases, HCC is preceded by liver cirrhosis indicating that the latter is an absolute requirement for HCV-associated liver cancer development. Various viral factors have also been postulated to be directly involved. Possible approaches to preventing HCV-related HCC include the development of a prophylactic vaccine to prevent the development of persistent infection following virus exposure, as well as therapeutic vaccines to either slow the progression of liver disease or to eradicate viral infection through the boosting of viral-specific **humoral** and cellular **immune** responses. Since the outcome of the standard-of-care treatment for chronic HCV patients (a combination of interferon-alpha and the guanosine analog **ribavirin**) appears to be dependent in part on the quality and quantity of both HCV-specific **humoral** and cellular **immune** responses, a therapeutic vaccine may be most effective when used as an adjunct with these and future antiviral drugs. A prophylactic vaccine comprising recombinant envelope glycoproteins E1 and E2 has been shown to prevent the development of persistent infection following exptl. challenge with both homologous and heterologous viral inocula in vaccinated chimpanzees, which represent the only animal model available. A related vaccine formulation is about to enter clin. trials in the USA. This vaccine primes the induction of anti-envelope antibodies as well as CD4+ T helper responses and may also be of value in treating chronically-infected patients with liver disease. In addition, we have been investigating methods to prime and boost HCV-specific cytotoxic lymphocytes (CTLs) capable of killing infected hepatocytes as well as secreting antiviral cytokines which are

therefore of potential therapeutic value. One effective method is the combination of the ISCOMs **adjuvant** (CSL Ltd) with a variety of recombinant HCV proteins. In rhesus macaques, a core protein adjuvanted with ISCOMs was shown to be very effective at priming core-specific Th1-like CD4+ T cells as well as CD8+ CTLs. Recently, this work has been extended to a large yeast-derived HCV polyprotein comprising the nonstructural proteins 3, 4 & 5 fused to the core protein. When adjuvanted with ISCOMs, strong multispecific T helper and CTL responses have been elicited in vaccinated chimpanzees that were superior to those elicited by various HCV DNA vaccine formulations.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:657357 CAPLUS
DOCUMENT NUMBER: 140:86787
TITLE: Pentoxifylline and severe acute respiratory syndrome (SARS): A drug to be considered
AUTHOR(S): Bermejo Martin, Jesus Fco; Jimenez, Jose Luis; Munoz-Fernandez, M. Angeles
CORPORATE SOURCE: Inmunobiologia Molecular, Hospital Gregorio Maranon, Madrid, Spain
SOURCE: Medical Science Monitor (2003), 9(6), SR29-SR34
CODEN: MSMOFR; ISSN: 1234-1010
PUBLISHER: International Scientific Literature, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The recent outbreak of Severe Acute Respiratory Syndrome (SARS) as a new viral disease is causing a great concern for health authorities and general population. Very little is known about the infectious agent (a coronavirus) and its etiopathol., having no specific treatment yet. Proinflammatory cytokines released by stimulated macrophages in the alveoli could have a prominent role in pathogenesis of SARS. Current treatment of SARS with antiviral agents such as **ribavirin** and corticosteroids have not achieved very satisfactory results. Corticosteroids exert an antiinflammatory effect and are indicated for the treatment of respiratory distress, but, on the other hand, they exert an immunosuppressor effect on **humoral** and cellular arms of the **immune** system. Based on previous reports and on our own experience in HIV, we propose here pentoxifylline (PTX), a drug commonly used in vascular indications, as a possible treatment for SARS due to its interesting properties. PTX would feature a possible antiviral activity along with a well-known cytokine-modulating activity not as immunosuppressant as that of the corticoids, down-regulating proinflammatory cytokines but leaving functional the rest of the immune response. Other effects of PTX are discussed, such as bronchodilation. The antiinflammatory, antiviral, immunomodulatory and bronchodilatory effects of PTX, along with its low cost and toxicity, make it a promising drug to be considered for SARS treatment, alone or as an **adjuvant** therapy in combination with other drugs. The classical antiviral approach as single treatment for viral diseases should be reviewed in this occasion; immunomodulatory therapies could play an important role in SARS therapy.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L9 IBIB ABS 1-2

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:997248 CAPLUS
TITLE: Hepatitis C vaccines to prevent liver cancer
AUTHOR(S): Houghton, M.
CORPORATE SOURCE: Chiron Corporation, Emeryville, CA, USA
SOURCE: Developments in Biologicals (Basel, Switzerland) (2004), 116(Development of Therapeutic Cancer Vaccines), 191-192
CODEN: DBEIAI; ISSN: 1424-6074
PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The hepatitis C virus (HCV) infects .apprx. 170 million individuals world-wide with a substantial annual incidence of new infections. At least 50% of infections become persistent and while most are relatively asymptomatic, there is a significant risk of a sequential progression to chronic active hepatitis, liver cirrhosis and then hepatocellular carcinoma (HCC). In Japan, HCV is the major risk factor for HCC. In essentially all cases, HCC is preceded by liver cirrhosis indicating that the latter is an absolute requirement for HCV-associated liver cancer development. Various viral factors have also been postulated to be directly involved. Possible approaches to preventing HCV-related HCC include the development of a prophylactic vaccine to prevent the development of persistent infection following virus exposure, as well as therapeutic vaccines to either slow the progression of liver disease or to eradicate viral infection through the boosting of viral-specific humoral and **cellular immune** responses. Since the outcome of the standard-of-care treatment for chronic HCV patients (a combination of interferon-alpha and the guanosine analog **ribavirin**) appears to be dependent in part on the quality and quantity of both HCV-specific humoral and **cellular immune** responses, a therapeutic vaccine may be most effective when used as an adjunct with these and future antiviral drugs. A prophylactic vaccine comprising recombinant envelope glycoproteins E1 and E2 has been shown to prevent the development of persistent infection following exptl. challenge with both homologous and heterologous viral inocula in vaccinated chimpanzees, which represent the only animal model available. A related vaccine formulation is about to enter clin. trials in the USA. This vaccine primes the induction of anti-envelope antibodies as well as CD4+ T helper responses and may also be of value in treating chronically-infected patients with liver disease. In addition, we have been investigating methods to prime and boost HCV-specific cytotoxic lymphocytes (CTLs) capable of killing infected hepatocytes as well as secreting antiviral cytokines which are therefore of potential therapeutic value. One effective method is the combination of the ISCOMs **adjuvant** (CSL Ltd) with a variety of recombinant HCV proteins. In rhesus macaques, a core protein adjuvanted with ISCOMs was shown to be very effective at priming core-specific Th1-like CD4+ T cells as well as CD8+ CTLs. Recently, this work has been extended to a large yeast-derived HCV polyprotein comprising the nonstructural proteins 3, 4 & 5 fused to the core protein. When adjuvanted with ISCOMs, strong multispecific T helper and CTL responses have been elicited in vaccinated chimpanzees that were superior to those elicited by various HCV DNA vaccine formulations.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:657357 CAPLUS
DOCUMENT NUMBER: 140:86787
TITLE: Pentoxifylline and severe acute respiratory syndrome (SARS): A drug to be considered
AUTHOR(S): Bermejo Martin, Jesus Fco; Jimenez, Jose Luis; Munoz-Fernandez, M. Angeles
CORPORATE SOURCE: Inmunobiologia Molecular, Hospital Gregorio Maranon, Madrid, Spain
SOURCE: Medical Science Monitor (2003), 9(6), SR29-SR34
CODEN: MSMOFR; ISSN: 1234-1010
PUBLISHER: International Scientific Literature, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The recent outbreak of Severe Acute Respiratory Syndrome (SARS) as a new viral disease is causing a great concern for health authorities and general population. Very little is known about the infectious agent (a coronavirus) and its etiopathol., having no specific treatment yet. Proinflammatory cytokines released by stimulated macrophages in the alveoli could have a prominent role in pathogenesis of SARS. Current treatment of SARS with antiviral agents such as **ribavirin** and corticosteroids have not achieved very satisfactory results. Corticosteroids exert an antiinflammatory effect and are indicated for the

treatment of respiratory distress, but, on the other hand, they exert an immunosuppressor effect on humoral and **cellular** arms of the **immune** system. Based on previous reports and on our own experience in HIV, we propose here pentoxifylline (PTX), a drug commonly used in vascular indications, as a possible treatment for SARS due to its interesting properties. PTX would feature a possible antiviral activity along with a well-known cytokine-modulating activity not as immunosuppressant as that of the corticoids, down-regulating proinflammatory cytokines but leaving functional the rest of the immune response. Other effects of PTX are discussed, such as bronchodilation. The antiinflammatory, antiviral, immunomodulatory and bronchodilatory effects of PTX, along with its low cost and toxicity, make it a promising drug to be considered for SARS treatment, alone or as an **adjuvant** therapy in combination with other drugs. The classical antiviral approach as single treatment for viral diseases should be reviewed in this occasion; immunomodulatory therapies could play an important role in SARS therapy.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT